REMARKS

Claims 1, 7, 10-27, 54-57, 59 and 60 are pending in the application. Claims 1, 7, 10-27, 54-57, 59 and 60 have been rejected. Claims 1, 12, 16, 54, 55, 56, 60 and 61 have been amended. New claim 63 has been added.

The amendments to the claims, specification and abstract and the incorporation of new claims are editorial in nature and contain no new matter.

the change has been to recite an oligonucleotide of claim 14, wherein the **detectable marker** is a radioactive, colorimetric, luminescent, fluorescent marker or gold label, a change from one that previously referred to the oligonucleotide of claim 13, which recited an oligonucleotide comprising DNA or RNA, which is a radioactive, colorimetric, luminescent, fluorescent marker or gold label. The amendment is editorial in nature, and reference to radioactive, colorimetric, luminescent, etc. detectable markers is fully supported in the specification at Page 31, lines 11-18, Page 55 lines 19-22.

Further, the amendment to claim 24, referring to the vector of claim 19, wherein the regulatory element is a Rous Sarcoma virus promoter does not constitute new matter, nor require further consideration, as it depends from claim 19, which recites a vector of claim 18, further comprising an regulatory element linked to the nucleic acid molecule. The change in dependency in claim 20 is similarly editorial in nature, and does not constitute new matter. Both changes are fully supported in the Specification at Page 18, lines 7-12 and Page 21, lines 13-15.

Claims 54-56 recite isolated nucleic acid moleculs of claim 1, wherein the nucleic acid sequence shares at least 75, 85 or 95% identity with the nucleic acid sequence of SEQ ID

NO: 1 does not constitute new matter, as it is fully supported in the Specification at Page 10, lines 18-25, and Page lines 17-19.

Claim 59 recites an isolated nucleic acid molecule of claim 7, wherein the claimed DNA is cDNA or genomic DNA. The change in dependency is editorial in nature, and is fully supported in the specification at Page 10, lines 29-30. The change therefore should not require any further consideration, and does not constitute new matter.

Newly added claim 63, which recites an oligonucleotide of at least 15 nucleotides capable of specifically hybridizing with a nucleic acid molecule encoding for a variant, analog or mutant of the mammalian p-Hyde protein is supported therein as well, in reference to oligonucleotides which specifically hybridize with the nucleic acids of the invention. Nucleic acids encoding for a variant, analog or mutant of the mammalian p-Hyde protein, as recited in claim 63, and referred to in claim 62 as described hereinabove, is supported at Page 10, lines 11-15, Page 13, lines 22-35-Page 14, lines 1-18, and Page 17, lines 5-28.

Thus all of the proposed amendments to the claims, and newly added claims are fully supported in the Specification, and do not constitute any new matter, accordingly, Applicants respectfully request entry of the Amendment.

PRIORITY

In the Office Action, the Examiner objected to the granting of the benefit of priority to the Subject Application from United States non-Provisional Application No. 09/302,457, filed on April 29, 1999. The Examiner alleged that the elected subject matter, namely the identification of a human homologue of the p-Hyde gene and its product, has priority dating back to the filing date of the instant application, alone. Applicants respectfully disagree. In United States non-Provisional Application No. 09/302,457, Applicants clearly show the identification of a human p-Hyde gene homologue (figures 8, 9 and 19A). Thus Applicants request that the Examiner withdraw his objection.

CLAIM REJECTIONS - 35 U.S.C. 112 SECOND PARAGRAPH

In the Office Action, the Examiner asserted that claims 1, 7, 10-27, 54-57, and 59-60 are rejected under 35 U.S.C. 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, by referring to the term "analogs".

In response, Applicants have amended claims 1, 7, 10-27, 54-57, and 59-60, removing

It is respectfully asserted that the foregoing amendment merely addresses matters of form and does not change the literal scope of the claim in any way or result in any prosecution history estoppel. Therefore Applicants respectfully request Examiner withdraws the rejection.

Applicants have, however, entered Claims 61 and 63, which recite analogs of the p-Hyde sequence. Applicants submit that the term "analogs" is defined in the Specification of the Subject Application, and is well known to the skilled person in the art. Applicants have specifically stated in the Specification in the Paragraph on Page 13, lines 22 - Page 14 line 6, that:

> The nucleotide encoding p-Hyde includes RNA, cDNA, genomic DNA, synthetic forms, and mixed polymers, both sense and antisense strands and may be chemically or biochemically modified or may contain non-natural or derivatized nucleotide bases, as will be readily appreciated by those skilled in the art. Such modifications include, for example, labels, methylation, substitution of one or more of the naturally occurring nucleotides with an analog, internucleotide modifications such as uncharged linkages (e.g., methyl phosphonates, phosphotriesters, phosphoamidates, carbamates, etc.), charged linkages (e.g., phosphorothioates, phosphorodithioates, etc.), pendent moieties (e.g., polypeptides), intercalators (e.g., acridine, psoralen, etc.), chelators, alkylators, and modified linkages (e.g., alpha anomeric nucleic acids, etc.). Also included are synthetic molecules that

> mimic nucleotides in their ability to bind to a designated sequence via hydrogen bonding and other chemical interactions. Such molecules are known in the art and include, for example, those in which peptide linkages substitute for phosphate linkages in the backbone of the molecule, substantially homologous to primary structural sequence but which include, e.g., in vivo or in vitro chemical and biochemical modifications or which incorporate

Applicants further characterize the p-Hyde proteins by the nucleic acids encoding such proteins, as well as by protein sequences comprising such proteins, including any other sequences, which have 75-95% similarity/identity with disclosed sequences. Thus, Applicants have specified the metes and bou
assertion, and Applicants respectfully request the Examiner to consider these arguments and withdraw the rejection.

Moreover, new Claims 61 and 63, which refer to isolated nucleic acid molecules of claim 1, having, or hybridizing with, a nucleic acid sequence encoding for a variant, analog or mutant of the human p-Hyde protein. As disclosed above, Applicants described the nucleic acid sequences encoding the p-Hyde protein as comprising an analog of the sequence (Page 13, lines 22-25), as defined hereinabove, with appropriate and definite description of particular modifications that comprise what is understood by those skilled in the art to comprise analogs and variants, such as for example: chemical or biochemical modification or the incorporation of non-natural or derivatized nucleotide bases, as will be readily appreciated by those skilled in the art.

> The nucleotide encoding p- ***chemically or biochemically modified or may contain non-natural or derivatized nucleotide bases***, as will be readily appreciated by those skilled in the art. Such modifications include, for example, labels, methylation, ***substitution of one or more of the naturally occurring nucleotides with an analog***

Applicants maintain that mutants of the disclosed species can be reasonably predicted by Applicants description, as well. Applicants indicate a role for p-Hyde involvement in tumor

suppression and induction of apoptosis. Applicants therefore describe in the Specification (Page 15, lines 5-11):

> -Hyde locus may be involved in the initiation and/or progression of other types of tumors. The locus is indicated in part by mutations that predispose individuals to develop cancer. These mutations fall within the p-Hyde region described infra. The p-Hyde locus is intended to include coding sequences, intervening sequences and regulatory elements controlling transcription and/or translation. The p-Hyde locus is intended to include all allelic variat

Applicants maintain that a structural and functional limitation exists in the newly submitted claim, that of mutations that alter p-Hyde expression or function, which are fully supported in the Specification of the Subject Application.

Thus, Applicants adequately describe analogs, fragments, variants and mutants and the structure of the genomic DNA related to the disclosed species as to how they may be reasonably predicted by one of skill in the art, using only the disclosed species as guides. Applicants thus respectfully request that the Examiner consider these arguments, and allow claims 61 and 63.

In the Office Action, the Examiner rejected claim 16 under 35 U.S.C. 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, by referring to the term 16 to refer to an isolated nucleic acid molecule having a nucleic acid sequence that is complementary to the nucleic acid sequence set forth in SEQ ID No. 1.

Both Claims 1 and 16 refer to a nucleic acid molecule. The Examiner objected to the nucleic acid molecule of claim 1 as allegedly encompassing DNA, which is double stranded

Applicants respectfully point out that as described in the specification on page 15 (lines 13-16), Applicants define a **nucleic acid** as comprising an **RNA** or **DNA** molecule in **either single** or **double stranded form**. Applicants claims to a complementary sequence, therefore recites **complementary RNA or DNA** which may be a single stranded DNA or RNA molecule with a nucleotide sequence that is complementary to the sequence as set forth in SEQ ID NO: 1. Therefore Applicants respectfully request that the Examiner reconsider and withdraw the rejection.

In the Office Action, the Examiner rejected claims 21-24 under 35 U.S.C. 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, by referring to the abbreviations "BAC".

In response, claim 21 has been amended. It is respectfully asserted that the foregoing amendment merely addresses matters of form and does not change the literal scope of the claim in any way or result in any prosecution history estoppel. Thus Applicants respectfully request that the Examiner reconsider and withdraw the rejection.

CLAIM REJECTIONS - 35 U.S.C. 112 FIRST PARAGRAPH

In the Office Action, the Examiner rejected claims 1, 7, 10-27, 54-56 and 59 under 35 U.S.C. 112, first paragraph as allegedly failing to clearly define a structural limitation of the claimed nucleic acid sequences. In response, Applicants have hereby amended claims 1, 7, 10-27, 54-56 and 59 to refer to an isolated nucleic acid molecule, comprising a nucleic acid sequence encoding a mammalian p-Hyde protein, with a nucleic acid sequence as set forth in SEQ ID No. 1. Applicants submit that the amended claims are thus definite, and respectfully request that the Examiner withdraw the rejection.

CLAIM REJECTIONS - 35 U.S.C. 101

In the Office Action, the Examiner rejected claims 1, 7, 10-27, 54-57 and 59-60 under 35 U.S.C. 101 as allegedly lacking patentable utility. Applicants respectfully traverse the Examiner's rejection. Applicants submit that the subject matter defined by the claims, namely the isolated nucleic acid molecule set forth in SEQ ID No. 1 is functionally characterized in the subject Application. Applicants have presented evidence in the Subject Application demonstrating an ability of a protein encoded by homologues/sequences of the Subject Application to induce cell-death-susceptibility in prostate cancer cells. Although the Examiner asserted that the rat p-Hyde protein has credible utility, the Examiner stated that:

a

Applicants respectfully disagree. Applicants submit that differential p-Hyde expression was evident in both rat and human prostate cancer cells, and that the sequences are highly homologous. If the gene product functions were unrelated, there would be no expectation for a comparable pattern of gene expression. Applicants therefore submit that comparable function and thereby utility has been demonstrated in the subject Application. Therefore, the claimed isolated nucleic acid molecule has a credible patentable utility. Accordingly, Applicants respectfully request that the rejection of claims 1, 7, 10-27, 54-57 and 59-60 under 35 U.S.C. 101 be withdrawn.

Claims Objections

The Examiner asserted that Claim 7 is objected to for having an improper Markush group. According to the Examiner the members of a Markush group must be independent and non-

Markush group is improper.

In response Applicants have previously amended Claim 7. Thus, claim 7 no longer contains an improper Markush group, and accordingly, Applicants respectfully request withdrawal of the rejection.

The Examiner objected to Claims 12-17 under 37 C.F.R. 1.75 (c), as being allegedly of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim (s), or amend the claims (s) to place the claims(s) in proper depended form, or rewrite the claim(s) in independent form. According to the Examiner Claims 12-17 are drawn to complementary or antisense sequences, none of which are encompassed by Claim 1, as amended.

In response Applicants have previously amended Claims 12-16 and cancelled claim 17. Claim 12 is an independent claim, referring to an oligonucleotide specifically hybridizing with a nucleic acid molecule encoding a mammalian p-Hyde protein, wherein the nucleic acid molecule has a sequence as set forth in SEQ ID No: 1, with claims 13-15 dependent therefrom, and claim 16 is an independent claim, referring to an isolated nucleic acid molecule having a nucleic acid sequence complementary to the sequence as set forth in SEQ ID No: 1. It is respectfully asserted that the foregoing amendment merely addresses matters of form and does not change the literal scope of the claims in any way or result in any prosecution history estoppel. Thus, Applicants have rewritten the claims in proper independent form, and accordingly, Applicants respectfully request withdrawal of the rejection.

The Examiner asserted that Claim 14 is objected to for having allegedly an improper format and for being inconsistent with previous claims. A period is required at the end of the claim. Also, the claim should depend from Claim 14 and cite wherein the detectable marker

In response Applicants have previously amended Claim 14. Thus amended Claim 14 has a proper format, and is now consistent with previous claims. Accordingly, Applicants respectfully request withdrawal of the rejection.

The Examiner asserted that Claim 59 is objected to for allegedly depending from a non-elected claim, Claim 53.

In response Applicants have previously amended Claim 59 to depend from claim 7. Thus Claim 59 properly depends from an elected claim. Accordingly, Applicants respectfully request withdrawal of the rejection.

REJECTIONS ON 35 U.S.C. 102

In the Office Action, the Examiner rejected claims 1, 7, 12, 13, 16 and 17 under 35 U.S.C. 102(b), as allegedly being anticipated by Hillier et al. In response, Applicants respectfully traverse this rejection in view of the remarks that follow.

Claim 1 has been herein amended to recite an isolated nucleic acid molecule encoding for a human p-Hyde protein comprising a nucleic acid sequence as set forth in SEQ ID No. 1. The Examiner has asserted that Hillier et al. disclose "a human mRNA EST sequence that matches 155 nucleotides of Applicants' SEQ ID No: 1", yet does not comprise the sequence in its entirety, and therefore Hillier et al., does not anticipate claim 1.

The nucleotide sequence disclosed by Hillier et al., is not a p-Hyde coding sequence as set forth in SEQ ID No. 1. In order for Hillier et al to be anticipatory of claim 12, the Hillier nucleotide sequence must disclose the p-Hyde coding sequence. Hillier et al., do not disclose oligonucleotides per se, and do not disclose a sequence encoding p-Hyde, as the sequence disclosed by Hillier et al does not in fact code for a functional protein. Thus Applicants submit that Hillier et al., does not anticipate claims 1 or 12.

Claim 16 has been amended to recite an isolated nucleic acid molecule comprising a nucleic acid sequence complementary to that set forth in SEQ ID No. 1. As in claim 1,

Hillier et al do not disclose the full p-Hyde coding sequence, and hence does not anticipate claim 16.

Claim 17 has been cancelled.

Applicants respectfully assert that amended independent claims 1, and dependent claim 7, 12 and dependent claim 13, and 16, are allowable. Accordingly, Applicants respectfully request that the Examiner withdraw the rejections to claims 1, 7, 12, 13 and 16.

Further, in the Office Action, the Examiner rejected claims 1, 7, 10-21, 25-27, 54-56 and 59 under 35 U.S.C. 102(b), as being anticipated by Talerman et al. In response, Applicants respectfully traverse this rejection in view of the remarks that follow.

ce that is 72%

. Claim 1 has been herein amended to recite an isolated nucleic acid molecule encoding for a human p-Hyde protein having a nucleic acid sequence as set forth in SEQ ID No. 1. The Examiner has asserted that Talerman et al. does not comprise the complete sequence as set forth in SEQ ID No. 1. The nucleotide sequence disclosed by Talerman et al., does not encode for p-Hyde, and, moreover, is not functionally comparable. Talerman et al discloses TSAP sequences, which are known to function in upregulation of apoptosis in a p53-dependent manner, following p53 induction. In the instant invention, however, p-Hyde functions through a different mechanism, acting as both a tumor suppressor, and as an apoptotic inducer, via its ability to impair DNA repair enzyme function. Talerman et al do not disclose a molecule that functions to impair DNA repair enzyme function. Thus functionally, and structurally, TSAP as disclosed by Talerman et al., differs from the instant invention, and therefore does not anticipate Claim 1, or dependent claims thereof. Claims 7, 10, 11, 18-21, 25-27 and 59 directly depend from claim 1, and therefore Applicants maintain is not anticipated by Tallerman et al., accordingly.

Claim 12 has been amended to recite an oligonucleotide of at least 15 bases capable of specifically hybridizing with a nucleic acid molecule encoding a mammalian p-Hyde protein comprising a sequence as set forth in SEQ ID No. 1. In order for Talerman et al to be anticipatory of claim 12, the nucleotide sequence disclosed by Talerman et al. must teach the nucleotide sequences from which an oligonucleotide specifically hybridizing with a nucleic acid sequence encoding for p-Hyde protein are designed. Talerman et al., do not teach a sequence encoding p-Hyde, thus Applicants submit that Talerman et al., does not anticipate claim 12. Claims 13-15 directly depend from claim 12, and therefore Applicants maintain is not anticipated by Talerman, et al., accordingly.

Claim 16 has been amended to recite an isolated nucleic acid molecule comprising a nucleic acid sequence complementary to that set forth in SEQ ID No. 1. As in claim 1, Talerman et al., do not disclose a sequence encoding p-Hyde, and hence do not anticipate claim 16. Accordingly, Applicants respectfully assert that amended independent claim 16 is allowable.

The Examiner has stated that Tallerman et al. anticipates claims 54-56. Claims 54-56 recite a nucleic acid molecule of claim 1, with the further restriction that the nucleic acid sequence share at least 75 %, at least 85% or at least 95% identity with p-Hyde. The Examiner has in fact indicated that the greatest degree of identity is 39%, and only a 72% similarity. Similarity implies functional comparability, which Applicants submit is absent in Tallerman et al., further, Applicants least degree of identity claimed is 75 %, well above the values for both sequence identity and similarity, as claimed by Tallerman et al.

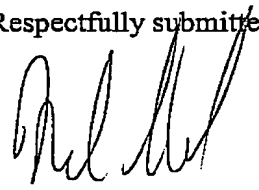
Therefore, Applicants respectfully assert that claims 1, 7, 10-21, 25-27, 54-56 and 59 are allowable. Accordingly, Applicants respectfully request that the Examiner withdraw the objections to the claims.

In view of the foregoing amendments and remarks, the pending claims are deemed to be allowable. Their favorable reconsideration and allowance is respectfully requested.

Should the Examiner have any question or comment as to the form, content or entry of this Amendment, the Examiner is requested to contact the undersigned at the telephone number below. Similarly, if there are any further issues yet to be resolved to advance the prosecution of this application to issue, the Examiner is requested to telephone the undersigned counsel.

Please charge any fees associated with this paper to deposit account No. 05-0649.

Respectfully submitted,



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